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From the Executive Editor

Trials and tribulations

There is a hierarchy of evidence relating to clinical research, extending from meta-analyses and randomised controlled trials to case reports and clinical anecdote.[1] Randomised controlled trials are not the only evidence that can be used to assess new interventions, but they are unarguably the best and most rigorous. Observational studies are helpful, and may lead to the same conclusion as randomised controlled trials,[2] but such studies are not accepted as definitive evidence of the efficacy of one treatment compared to another.[3] Effective use of randomised controlled trials has revolutionised many areas of healthcare, not the least the treatment of cardiac disease in adults.[4]

Over the last decade, we too have seen remarkable advances in the treatment of children with congenital cardiac disease, many of them chronicled in the pages of *Cardiology in the Young*. Our practice has changed, the care of our patients has become better, and outcomes have improved. But where are the clinical trials that led to these changes? It is easy for us to be complacent about the progress we have made. We see patients in our clinics everyday, and we know that they are doing better than they would have only a few years ago. In the face of this, why should we worry about the finer points of evidence-based medicine? At a meeting I attended recently, one of the delegates, frustrated by the calls for clinical trials, raced to the microphone to say, "If we relied on clinical trials, we would never have introduced the arterial switch operation!" A good point, and one that reaches to the very heart of the issue.

It is now 28 years since Jatene described the first successful arterial switch operation,[5] but we still do not know whether the procedure achieves better long-term results that the atrial re-directive operations it supplanted. We know that its introduction was accompanied by an increase in surgical mortality compared to contemporary Senning and Mustard operations.[6] We also know that, as technical skills have advanced, it can now be done with an acceptable short-term mortality.[7] But does it give children with transposition a better long-term chance of good health than did the earlier alternatives? We do not know. There has been no randomised controlled trial which compares the outcome for the arterial switch and atrial repair for transposition. In particular, there is no cohort of patients undergoing surgery at the same time by the two techniques being followed to compare the results over the long-term. Thus, for a relatively common and consistent congenital cardiac malformation, we have no evidence for the best operative approach. Sadly, it seems unlikely now that we will ever have this evidence. The delegate was right. If we had undertaken clinical trials, we might never have introduced the arterial switch operation. The trouble is, we do not know whether that would have been a good or bad thing.

The last few years have seen rapid progress in the development of devices to close intracardiac septal defects. When a parent asks, which is the best option for their child with an atrial septal defect, surgery or transcatheter closure, what answer should we give? It is self-evident that transcatheter occlusion is likely to be less traumatic for the child, and for many parents the more attractive option, but where is the evidence that it leads us to believe that the results are as good or better than surgery? Looking through the literature, the best I could find was a non-randomised trial.[8] There is, then, only equivocal evidence for the current optimal treatment of what is one of the most common congenital cardiac defects. In most other clinical specialities, such evidence would be regarded as inadequate to support the introduction of a new therapy. It is not too late to compare these two approaches for closure of atrial septal defects, but history does not suggest it will happen. In the past, lack of a randomised controlled trial has never been allowed to delay the introduction of new interventional procedures.

It is possible to identify at least two examples of common defects, therefore, where we should have been able to marshal strong evidence to support the introduction of new therapies. In fact, our practice has changed on the basis of anecdotal evidence and professional consensus. There are, of course, many other cardiac anomalies that are much less common where we have to make decisions concerning treatment on even weaker evidence. Indeed, a trawl through the literature shows that there are very few randomised controlled trials for congenital cardiac disease as an entity. For some reason, the ethos of

evidence-based medicine does not seem to have much impact on our particular specialty. Many excuses are advocated to support this deficiency. Some are rational, such as the very long-term follow up required, the rarity and variability of some conditions, the ethics of randomisation, and the logistical problems of organising multi-centric trials. These issues all present problems, but no more than in other specialties where they have been overcome. Statistical methods that enable trials to be undertaken for rare conditions are well established.[9] Multi-centric randomised trials are routine in many medical specialties that face exactly similar problems.

These are the excuses, but there are other reasons that reflect the culture of our specialty. Innovative individuals often become strong advocates of the approach they introduce, be it a new operative technique or a new interventional procedure. Calls for randomised trials are often swept aside in the enthusiasm for the new. Trials are seen as only delaying the self-evident benefit of the innovation for our patients. But what is self-evident may be wrong. The history of medicine is littered with self-evident truths that turn out to be counterfeit. We let down our patients, and we let down ourselves, if we do not use the best possible evidence to evaluate the methods we use for treating congenital cardiac malformations. Randomised controlled trials are possible in paediatric cardiology. Two examples have been published recently,[10,11] but they are few, and there are none that address the major innovations of treatment in the last few years. *Cardiology in the Young* would like to publish high quality clinical trials that answer fundamental clinical questions. If you would like to argue for a multi-centric trial to investigate a specific clinical question, let us know. We can guarantee our support.

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